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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	14

DATE MAILED: 04/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,615	JOHANSEN ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,35 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20, 35 and 36* is/are rejected.

7)☒ Claim(s) *35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 March 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Claims 1-54 were pending in the application and were subject to restriction in Paper No. 8, dated 9/3/02. In Paper No. 12, filed 2/3/03, Applicants elected Group I, claims 1-20, 35 and 36. Applicants also cancelled claims 21-34 and 37-54. Since Applicants did not provide any arguments regarding this restriction, it will be treated as an election without traverse. Therefore, this restriction is deemed proper and is made FINAL.

B. The Information Disclosure Statement, filed 8/30/01, has been entered into the record.

C. The Information Disclosure Statement, filed 2/7/03, has been entered into the record.

2. Information Disclosure Statement

A. Reference C22 on the Form PTO-1449 filed 8/30/01 and reference C27 on the Form PTO-1449 filed 2/7/03 have been lined through. Reference C22 does not cite a date of deposit. The International Search Report of Reference C27 is not a proper citation for an IDS.

3. Oath/Declaration

A. Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). On the first page, the words "as USSN 09/804,615" have been written. In addition, the paragraph beginning with "I hereby claim" recites 60/097,774 twice, with two different filing dates, and does not reference 60/092,229.

4. Specification

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The word "novel" should be removed from the title since all patents claim novel subject matter.

B. Figures 4 and 5 are objected to since the Brief Description of Drawings recites panels A-C for Figure 4 and panels A and B for Figure 5. However, the Figures do not show these panels.

5. Priority Claim

A. The specification is objected to since the first line recites that the present application "claims priority to" USSN 09/347,613. This line should read "is a continuation-in-part of" if this is the case.

B. No foreign priority documents are present in this application. It is likely that parent application 09/347,613 contained these documents. However, this application was not accessible to the Examiner at the time of this Office Action. If Applicants have met the conditions for priority in the parent application (DE 1998 Application Nos. 01265, 01048, 00904), then a statement on the record is required, or a copy of these foreign documents will need to be submitted for this application.

6. Claim Objections

A. Claim 35 is objected to since it depends from non-elected claim 32.

7. Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

A. Claims 1-8, 10-13, 15-20, 35 and 36 are provisionally rejected under the judicially created doctrine of double patenting over one or more claims of copending Application No. 09/662,183. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: both applications claim neublastin polypeptides comprising all or part of SEQ ID NO:2 or 9, which have overlapping features. Claim 66 of '183 recites an isolated neublastin polypeptide similar to SEQ ID NO:2 with specific limitations. These limitations are met by SEQ ID NO:9 of the present

invention, regardless of whether or not the protein of SEQ ID NO:9 is truncated. The fact that SEQ ID NO:2 is shorter than SEQ ID NO:9 meets the limitation of a truncated protein, since the protein of SEQ ID NO:2 is, technically, missing amino-terminal residues of SEQ ID NO:9. Furthermore, the polypeptide of the present invention is either encoded for, or hybridizes to, the fragment of SEQ ID NO:1 recited in claim 67 of '183, especially due to the large degree of overlap in the two sequences, as well as the lack of any specific stringency conditions recited in the claim. In addition, the protein of SEQ ID NO:2 meets the limitations of claims 2-4 of the present invention since the proteins would be expected to dimerize and bind RET since they are both neublastins. Additionally, SEQ ID NO:2 meets the "% identity" and "essentially of" limitations of claims 5-8, 10-13 and 15 of the present invention. Similarly, the protein of SEQ ID NO:2 could be made using the methods of claims 16-20. Claims 15, 21, 37, 38, 42-44 of '183 are also included in this rejection since they recite "glycosylation" and "pharmaceutical compositions" of the claimed neublastin proteins, unless Applicants can specifically explain why these claims should not be included.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

8. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1-20, 35 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the truncated rat neuroblastins in Example 11 of the specification, does not reasonably provide enablement for all truncated neuroblastins, including those comprising only the "**seven cysteine residues of SEQ ID NO:9, residues 119-220, 122-220 of SEQ ID NO:9, or neuroblastins which are at least 70%-95% identical to these fragments, nor for any pharmaceutical compositions**" comprising any and all truncated neuroblastin polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of

experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to Applicants claiming all truncated neuroblastin polypeptides, even including those meeting the limitations of claims 2-4. Applicants have only apparently identified a mouse, rat and human neuroblastin. However, Applicants only provide guidance and working examples of a truncated rat neuoblastin protein (Example 11). The specification provides no guidance or working examples of truncated neuroblastin proteins from any other species, including human. The claims recite that these human truncates comprise residues 119-220 or 122-220 of SEQ ID NO:9, but Applicants have not shown that these truncation mutants have a function. The situation is the same for claiming all truncation mutants comprising only the cysteine residues of SEQ ID NO:9. Applicants have not provided examples of any proteins which comprise these cysteine residues other than SEQ ID NO:9, nor have they shown which residues are critical for receptor function, including for the functions recited in the claims, nor, respectfully, have they even demonstrated that the protein of SEQ ID NO:9 is functional. Simply stating that the protein must have cysteine residues does not provide the artisan with enough guidance to make a functional truncated neuroblastin, nor is it predictable to the artisan how to make a functional neuroblastin, or a truncated neuroblastin, given either no guidance, as in claims 1-3 for example, or the minimal guidance that the only limitation to make such a protein is that it must comprise 7 cysteine residues.

In addition, proteins which are "at least 70%-~~90~~95% identical" to the protein of SEQ ID NO:9, or to a fragment thereof, would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:9. Again, Applicants have not shown which residues are critical for receptor function, including for the functions recited in the claims, nor, respectfully, have they even demonstrated that the protein of SEQ ID NO:9 is functional, nor do, for example, do claims 1 and 5 even recite a function for the truncated protein. Furthermore, Applicants have not provided any guidance or working examples of how to use the claimed pharmaceutical compositions, whether or not these compositions comprise SEQ ID NO:9, or the excessive range of neuroblastins claimed. These compounds are neurotrophic factors, which must enter the brain to be effective. Proteins are not known to readily pass through the blood brain barrier and Applicants have not enabled such a method.

Finally, claims 1 and 16 recite "mature" neuroblastin. However, it is not known what the sequence of any and all mature neuroblastins is, including that of the protein of SEQ ID NO:9 is. It is

believed that the mature form of SEQ ID NO:9 is the 140 amino acid protein starting with residue number 1 in the sequence listing (i.e. beginning "Pro-Pro-Pro"). Applicants are requested to confirm this definition, or to specifically define what the sequence of the mature form is. However, the specific amino acid sequences of mature forms other than that of SEQ ID NO:9 would still not be known and, therefore, not enabled by the specification.

Therefore, in summary, the breadth is excessive regarding Applicants claiming all truncated neuroblastin proteins, including fragments thereof or those which are 70-95% identical to a fragment of SEQ ID NO:9, as well as pharmaceutical compositions thereof.. Applicants only provide guidance and working examples of a truncated rat neuroblastin and provide no guidance or working examples of how to make pharmaceutical compositions comprising truncated neuroblastins. Therefore, it is not predictable to the artisan what residues would be critical to maintain the function of a truncated neuroblastin, or how to make a pharmaceutical composition thereof. For these reasons, the Examiner has concluded that undue experimentation would be required to practice the invention as claimed.

9. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1-8, 10-13, 15-20 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Applicants are claiming all truncated neuroblastins, including those comprising only the "**seven cysteine residues of SEQ ID NO:9, residues 119-220, 122-220 of SEQ ID NO:9, or neuroblastins which are at least 70%-95% identical to these fragments, as well as pharmaceutical compositions**" comprising any and all truncated neuroblastin polypeptides. Applicants have purported to teach a human neuroblastin protein of SEQ ID NO:9. However, Applicants have not adequately described this protein, except by SEQ ID NO. The only adequately described neuroblastin protein is that of rat, which is not claimed. Therefore, even if Applicants adequately described a human neuroblastin, they have still not described all truncated neuroblastins, including those comprising only the "seven cysteine residues of SEQ ID NO:9, residues 119-220, 122-220 of SEQ ID NO:9, or neuroblastins which are at least 70%-95% identical to these fragments. These proteins would have one or more amino acid substitutions, deletions, insertions and or additions to the protein encoded for by SEQ ID NO:9 and Applicants have not demonstrated which residues are critical for protein function.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:9, alone is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

The specification provides a written description of only one neuroblastin (rat). Even if Applicants adequately described the full-length human neuroblastin of SEQ ID NO:9, one skilled in the art cannot reasonably visualize or predict critical amino acid residues which would structurally characterize the genus of neuroblastin proteins claimed, because it is unknown and not described what structurally constitutes any different neuroblastins, or neuroblastins from any different species, which, other than rat (the mouse neuroblastin has been disclosed in the specification, but nothing more than the SEQ ID NO is disclosed) are further not described, or any different amino acid sequence that is less, or other than, the full length of SEQ ID NO:9; thereby not meeting the written description requirement under 35 USC 112, first paragraph.

B. Claims 1 and 16 recite a "**mature neublastin polypeptide**." However, the instant specification fails to describe that portion of a protein which is the "mature" portion. Applicant is claiming a very specific species which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The structure of a "mature neublastin" cannot be predicted on the basis of the amino acid sequence of the entire protein since the protein may be proteolytically cleaved in vivo, as well as being differentially processed based on which in tissue the protein is expressed. The claims are directed to a species of protein, the structure of which cannot be determined or predicted from full-length amino acid sequence and the specification does not evidence isolation or conception of the structure of the "mature" form of a neublastin. Therefore, the specification does not provide an adequate written

description of a mature protein, and thus the claimed invention, to the extent that it reads upon mature protein was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 1-8, 10-13, 15-20, 35 and 36 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 09/662,183 which has a common inventor with the instant application (Johansen). Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application.

Both applications claim neublastin polypeptides comprising all or part of SEQ ID NO:2 or 9, which have overlapping features. Claim 66 of '183 recites an isolated neublastin polypeptide similar to SEQ ID NO:2 with specific limitations. These limitations are met by SEQ ID NO:9 of the present invention, regardless of whether or not the protein of SEQ ID NO:9 is truncated. The fact that SEQ ID NO:2 is shorter than SEQ ID NO:9 meets the limitation of a truncated protein, since the protein of SEQ ID NO:2 is, technically, missing amino-terminal residues of SEQ ID NO:9. Therefore, not only would it have been obvious to one of ordinary skill in the art at the time of the present invention to have made truncation mutants of SEQ ID NO:9 of the present invention in order to determine structure-function relationships, but, according to the limitations of the claims of the present invention, SEQ ID NO:2 would inherently read on the claims of the present invention since this protein is shorter than that of SEQ ID NO:9.

Furthermore, the polypeptide of the present invention is either encoded for, or hybridizes to, the fragment of SEQ ID NO:1 recited in claim 67 of '183, especially due to the large degree of overlap in the two sequences, as well as the lack of any specific stringency conditions recited in the claim. In addition, the protein of SEQ ID NO:2 meets the limitations of claims 2-4 of the present invention since the proteins

would be expected to dimerize and bind RET since they are both neublastins. Additionally, SEQ ID NO:2 meets the "% identity" and "essentially of" limitations of claims 5-8, 10-13 and 15 of the present invention. Similarly, the protein of SEQ ID NO:2 could be made using the methods of claims 16-20. Claims 15, 21, 37, 38, 42-44 of '183 are also included in this rejection since they recite "glycosylation" and "pharmaceutical compositions" of the neublastin protein.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned application 09/662,183, discussed above, presently forms the basis for a rejection of the noted claims under 35 U.S.C. 103(a) since the commonly assigned case appears to qualifys as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. Again, in order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will this rejection rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

11. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
March 31, 2003

ROBERT LANDSMAN
PATENT EXAMINER